Amendments to the Claims

Listing of the Claims

1. (Currently Amended) A nucleic acid construct comprising viral genomic nucleic acid where the viral genomic nucleic acid is (1) (i) herpes virus genomic nucleic acid or (ii) a nucleic acid sequence that has at least 80% sequence homology to a herpes virus genomic nucleic acid, and (2) comprises, ~~said viral genomic nucleic acid comprising~~ at least two endogenous gene expression regulatory units which each comprise an endogenous promoter that is capable of expression in a mammalian cell, where the endogenous promoters of the units ~~which~~ are active at the same phase in the herpes viral life cycle, wherein ~~of the virus the viral genomic nucleic acid is derived from,~~:

(a) the ~~at least two of the endogenous gene expression regulatory units comprising~~ promoters ~~active at the same phase~~ are each operably linked to a separate ~~heterologous~~ coding sequence ~~inserted into the viral genomic nucleic acid~~; [[and]]

(b) the viral genomic nucleic acid is from 1 to 50 kb in length ~~excluding the heterologous sequences inserted into it.~~; and

(c) more than 10% and up to 95% of the viral sequences which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid in the construct are absent from the construct.

2. (Currently Amended) A nucleic acid construct according to claim 1, wherein the ~~at least two~~ endogenous promoters are switched on at the same point in the ~~viral~~ herpes virus life cycle ~~of the virus the genomic nucleic acid is derived from~~.

3. (Currently amended) A nucleic acid construct according to claim 1, wherein the ~~at least two~~ endogenous gene expression regulatory units are ~~either both/all from~~ immediate early genes or ~~both/all from~~ early viral genes.

4. (Currently amended) A nucleic acid construct according to claim 1, wherein the ~~at least two~~ endogenous gene expression regulatory units are different to one another.

5.-6. (Canceled)

7. (Currently Amended) A nucleic acid construct according to claim [[6]] 1, wherein the herpes virus is ~~selected from the group consisting of a~~ herpes simplex virus (HSV)~~, a cytomegalovirus (CMV) and an Epstein Barr virus (EBV)~~.

8. (Original) A nucleic acid construct according to claim 7, wherein the HSV is selected from the group consisting of HSV-1 and HSV-2.

9. (Currently Amended) A nucleic acid construct according to claim 7, wherein the viral genomic nucleic acid is derived from a herpes simplex virus and the ~~at least two~~ endogenous gene expression regulatory units each comprise an endogenous promoter [[are]] selected from the group consisting of the ICP0, ICP4, ICP22 and ICP27 gene promoters.

10. (Currently amended) A nucleic acid construct according to claim 7, wherein the viral genomic nucleic acid is ~~derived~~ from a herpes simplex virus and the ~~two~~ endogenous promoters of the ~~at least two~~ gene expression regulatory units are HSV tegument protein gene promoters.

11. (Cancelled)

12. (Currently Amended) A nucleic acid construct according to claim 1, wherein all of the ~~heterologous~~ coding sequences expressed by the endogenous gene expression regulatory units are derived from the same organism.

13. (Currently Amended) A nucleic acid construct according to claim 1, wherein two or more of the ~~heterologous~~ coding sequences encode antigens.

14. (Original) A nucleic acid construct according to claim 1, wherein the antigens are antigens from a pathogen.

15. (Canceled)

16. (Currently Amended) A nucleic acid construct according to claim [[15]] 1, wherein the absent region of (c) comprises part or all of the intervening sequences between two of the adjacent endogenous gene expression regulatory units linked to ~~heterologous~~ coding sequences.

17. (Currently Amended) A nucleic acid construct according to claim [[15]] 1, wherein the absent region of (c) comprises ~~corresponds to~~ one or more of the genes present in the region of the viral genome other than those of the ~~at least two~~ endogenous gene expression regulatory units used to express the ~~heterologous~~ coding sequences.

18. (Currently Amended) A nucleic acid construct according to claim 16 [[15]], wherein the viral genomic nucleic acid is from HSV-2 and the viral sequences have been removed from the construct by one or more of the following techniques: (a) partial Eco RI

digestion and religation; (b) Bst 11071 and ScaI digestion and religation; (c) Nsi digestion and religation; ~~(a)~~ (d) a partial digestion with a BstXI enzyme and then religation to remove sequences between ICP27 and ICP0; ~~(b)~~ (e) a complete digestion with a BspHI enzyme, followed by a partial digestion with a BsiWI enzyme and then religation to remove sequences adjacent to ICP22; ~~(c)~~ (f) a digestion with a SrfI enzyme and then religation to remove sequences between ICP4 and ICP0; and ~~(d)~~ (g) total digestion with a BstXI enzyme and then religation to remove sequences beween ICP27 and ICP0.

19. (Currently Amended) A nucleic acid construct according to claim 16 [[15]], wherein the viral genomic nucleic acid is from HSV-1 and comprises the ICP 0, ICP 4, ICP 22 and ICP 27 promoters operably linked to their natural coding sequences ~~and the virual sequences have been removed from the construct to remove substantially all of the HSV-1 sequences extraneous to ICP0, ICP4, ICP22 and ICP27 coding sequences~~.

20. (Canceled)

21. (Currently Amended) A nucleic acid construct according to claim 1, wherein the endogenous gene expression regulatory units operably linked to the ~~heterologous~~ coding sequences are endogenous promoters.

22.-25. (Canceled)

26. (Currently Amended) Coated particles, suitable for delivery from a particle-mediated delivery device, which particles comprise carrier particles coated with the [[a]] nucleic acid construct of claim 1. ~~wherein the construct comprises viral genomic nucleic acid, said viral genomic nucleic acid comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter where the endogenous promoters of the units are active at the same point in the viral cycle of the virus the viral genomic nucleic acid is derived from, where: at least two of the endogenous gene expression regulatory units comprising gene expression regulatory units comprising promoters are each operably linked to a heterologous coding sequence inserted into the viral genomic nucleic acid; and the viral genomic nucleic acid is from 1 to 50 kb in length the heterologous sequences inserted into it.~~

27. (Original) Coated particles according to claim 26, wherein the carrier particles are gold or tungsten.

28. (Original) A dosage receptacle for a particle mediated delivery device comprising coated particles according to claim 26.

29. (Original) A particle mediated delivery device loaded with coated particles according to claim 26.

30. (Original) A particle mediated delivery device according to claim 29 which is a needleless syringe.

31. (Withdrawn - Currently Amended) A method of obtaining expression in a mammalian cell of a polypeptide of interest, which method comprises transferring into said cells a nucleic acid construct of claim 1. ~~comprising viral genomic nucleic acid, said viral genomic nucleic acid comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter where the endogenous promoters of the units are active at the same phase in the viral cycle of the virus the viral genomic nucleic acid is derived from, where: at least two of the endogenous gene expression regulatory units comprising promoters are each operably linked to a heterologous coding sequence inserted into the viral genomic nucleic acid; and the viral genomic nucleic acid is from 1 to 50 kb in length excluding the heterologous sequences inserted into it.~~

32. (Withdrawn) A method according to claim 31, wherein the construct is delivered directly into a subject.

33. (Withdrawn) A method according to claim 32, wherein the construct is delivered by injection, transdermal particle delivery, inhalation, topically, orally, intranasally or transmucosally.

34. (Withdrawn) A method according to claim 32, wherein the construct is delivered by needleless injection.

35. (Withdrawn) A method according to claim 34, wherein the nucleic acid construct is coated onto carrier particles.

36. (Withdrawn - Currently Amended) A method of nucleic acid immunisation comprising administering to a subject an effective amount of coated particles, which particles are suitable for delivery from a particle-mediated delivery device, the particles comprising carrier particles coated with a nucleic acid construct of claim 1. ~~wherein the construct comprises viral genomic nucleic acid, said viral genomic nucleic acid comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter where the endogenous promoters of the units are active at the same phase in the viral cycle of the virus the viral genomic nucleic acid is derived from, where: at least two of the endogenous gene expression regulatory units comprising promoters are~~

~~each operably linked to a heterologous coding sequence inserted into the viral genomic nucleic acid; and the viral genomic nucleic acid is from 1 to 50 kb in length excluding the heterologous sequences inserted into it.~~

37. (Currently Amended) A method of generating a nucleic acid construct for direct administration to a subject to elicit an immune response in the subject, the method comprising: (a) inserting herpes virus genomic nucleic acid or a sequence with at least 80% sequence homology ~~viral genomic nucleic acid~~ into a vector backbone, said viral genomic nucleic acid being from 1 to 50kb in length and comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter capable of expression in a mammalian cell, where the endogenous promoters of the units are active at the same phase in the herpes virus life ~~viral~~ cycle ~~of the virus the viral genomic nucleic acid is derived from;~~ and (b) either prior to, at the same time, or after inserting the viral genomic nucleic acid into the vector backbone, deleting from the viral genomic nucleic acid some or all of the viral sequences, apart from the at least two endogenous gene expression regulatory units, which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid of the construct so that more than 10% and up to 95% of the viral sequences which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid in the construct are absent from the construct ~~where the length of the viral genomic nucleic acid inserted into the vector backbone being from 1 to 50 kb~~.

38. (Currently Amended) A method according to claim 37, further comprising coating the constructs on particles suitable for delivery from a particle mediated delivery device ~~wherein the nucleic acid sequences deleted are part or all of the non-coding intervening sequences between two of the endogenous promoters~~.

39. (Original) Coated particles, suitable for delivery from a particle-mediated delivery device, which particles comprise carrier particles coated with a nucleic acid construct generated by a method as defined in claim 36.

40. (Original) A dosage receptacle for a particle mediated delivery device comprising coated particles according to claim 39.

41. (Original) A particle mediated delivery device loaded with coated particles according to claim 40.

42. (Withdrawn) A method of obtaining expression in a mammalian cell of a polypeptide of interest, which method comprises transferring into said cells a nucleic acid construct generated by a method according to claim 37.

43. (Withdrawn) A method of nucleic acid immunisation comprising administering to a subject an effective amount of coated particles, which particles are suitable for delivery from a particle-mediated delivery device, the particles comprising carrier particles coated with a nucleic acid construct generated by a method according to claim 37.

44. (Withdrawn-currently amended) Use of a nucleic acid construct ~~according to any one~~ of claim[s] 1 ~~to 21, a nucleic acid construct generated by a method according to any of the claims 22 to 25, 37 and 38 or coated particles according to any one of the claims 26, 27, and 39 in the manufacture of a medicament~~ for use in nucleic acid immunization.

45. (New) A nucleic acid construct according to claim 1, where the construct is a cosmid or a plasmid.

46. (New) A nucleic acid construct according to claim 1, wherein the construct lacks viral packaging sequences.

47. (New) A nucleic acid construct according to claim 1, wherein the construct lacks a viral origin of replication.

48. (New) A nucleic acid construct according to claim 1, where more than 20% and up to 85% of the viral genomic sequences are deleted.

49. (New) A nucleic acid construct according to claim 1, where more than 30% and up to 75% of the viral genomic sequences are deleted.

50. (New) A nucleic acid construct according to claim 1, where the endogenous expression regulatory units are operably linked to their natural coding sequences.

51. (New) A nucleic acid construct according to claim 1, wherein the sequence for more than 500bp upstream and downstream of the promoter of the endogenous gene expression units is identical to, or has at least 90% homology to, the endogenous sequences of the herpes virus genome.

52. (New) A nucleic acid construct according to claim 1, wherein two or more of the endogenous gene regulatory units are from consecutive genes in the herpes virus genome.

53. (New) A nucleic acid construct according to claim 9, wherein three or more of the endogenous gene regulatory units are from consecutive genes in the herpes virus genome.